Primary Extracranial Meningioma of the Foot: A Case Report

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We present a rare case of primary extracranial meningioma in a 36-year-old man, who had a solitary multinodular mass located in the plantar muscle of the foot. The histology of specimens from simple excision was typical of meningioma, showing bland spindle cell proliferation with a whorl pattern. Immunohistochemical analysis demonstrated that the tumor cells showed diffuse and strong positivity for epithelial membrane antigen as well as moderate reactivity for cytokeratin and vimentin. Ultrastructurally, the tumor cells were characterized by thin bipolar cytoplasmic processes and joined by multiple small desmosomes. There were frequent pinocytotic vesicles and a distinct external lamina on the cell surface. These findings suggest that this primary ectopic meningioma, arising in the soft tissue, may have been derived from perineurial cells of the peripheral nerve, but was morphologically distinguishable from perineurioma. Primary extracranial meningioma should be included in the differential diagnosis of soft-tissue spindle cell tumors, especially those of peripheral nerve origin.

Key words: meningioma – extracranial – perineurioma – ultrastructure – peripheral nerve

INTRODUCTION

Meningioma is a well-recognized tumor of the central nervous system. Extracranial non-dural or ectopic meningiomas are very rare and most reported cases in the English literature have arisen in the head and neck region (1–7). Even more rarely, primary meningiomas occur in the lung (8,9), mediastinum (10), skin (11,12) and soft tissue (13,14).

Here we present the third reported case of primary extracranial meningioma occurring in the soft tissue of the foot, describe the clinicopathological, immunohistochemical and ultrastructural features and discuss its possible histogenesis and differential diagnosis.

CASE REPORT

CLINICAL HISTORY

A 36-year-old man presented with a tumor mass in his left sole, which had been present for 10 years. The patient had been referred because the mass had become slightly larger and tender. On physical examination, the mass was located within the medial plantar muscle of the left foot. A multinodular mass, 1.5 cm in diameter, with a smooth margin was demonstrated by computed tomography (CT). Magnetic resonance imaging (MRI) revealed the lesion to be well circumscribed and lobulated with low signal intensity on T1-weighted imaging and with high signal intensity on T2-weighted imaging (Fig. 1a and b). The tumor was non-homogeneously enhanced by gadolinium (Fig. 1c). Results of blood analysis, blood chemistry and serum hormone levels were within normal limits. In March 1999, the patient underwent marginal excision of the mass. The tumor was surrounded by unclear and thin fibrous capsule, totally embedded within the striated muscle layer. The relationship of the tumor to peripheral nerves was not identified. After surgery, clinical investigations, including MRI, did not detect any another lesions. The patient has shown no signs of recurrence or metastasis during a follow-up period of 13 months.

HISTOLOGICAL FINDINGS

Histologically, the lesion was characterized by a lobular micro-architecture and showed uniform spindle cell proliferation separated by hyalinized collagen bundles (Fig. 2). The neoplastic cells had abundant lightly eosinophilic cytoplasm, indistinct cytoplasmic borders and round or oval nuclei with finely dispersed chromatin and indistinct nucleoli (Fig. 3). The spindle cells were often arranged in sweeping fascicles and concentrically wrapped in tight whorls. Nuclear clearing (pseudo-inclusion) was also common in these tumor cells. There were no psammoma bodies throughout the specimens. Atypical cells were minimal and there were 4 mitoses out of 10

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high-power fields [HPF] with no abnormal mitoses. Small foci of necrosis were seen.

IMMUNOHISTOCHEMICAL FINDINGS
Sections were used for immunohistochemical analysis by the standard avidin–biotin technique with the following primary antibodies: AE1/3 (cytokeratin), anti-epithelial membrane antigen (EMA), V9 (vimentin), D33 (desmin), 1A4 (α-smooth muscle actin), anti-S-100 protein, My10 (CD34), HECD-1 (E-cadherin), DO7 (p53) and MIB-1 (Ki-67). The tumor cells showed diffuse and strong reactivity for EMA (Fig. 4a). Many tumor cells were moderately positive for vimentin and cytokeratin (Fig. 4b). Desmin, α-smooth muscle actin, S-100 protein, CD34, E-cadherin and p53 were negative. The MIB-1 labeling index was 5%.

ULTRASTRUCTURAL FINDINGS
For ultrastructural examination, the paraffin-embedded tissue was deparaffinized with xylene and ethanol. Small minced fragments of the tissue were washed in 0.05 M phosphate-buffered saline, fixed in 2.5% glutaraldehyde, post-fixed in 1% osmium tetroxide and embedded in epoxy resin. Thin sections were stained with uranyl acetate and lead citrate. Ultrastructurally, the neoplastic cells were predominantly spindle-shaped with thin bipolar cytoplasmic processes that were often coated on both free surfaces by a distinct external lamina (Fig. 5). Pinocytotic vesicles were frequently observed on the cell surfaces. The cytoplasmic processes did not interdigitate with adjacent cells, but were joined by multiple small desmosomes (Fig. 6).

DISCUSSION
Meningiomas are one of the most common tumors of the central nervous system. They are derived from the arachnoid cells of the meninges. Rarely, ectopic meningiomas arise through metastatic spread, in the lung, liver, bone and lymph nodes, and are often seen with malignant variants (15–18). Primary extracranial meningiomas are even less common and
have been reported sporadically, mostly in the head and neck region, such as the scalp, nose, paranasal sinus and parotid gland (2–7) as well as in the lung (8,9), mediastinum (10), skin of the finger and eyelid (11,12), retroperitoneum (13) and the thigh muscle (14). In most cases, their morphological features are similar to those of a meningioma of the central nervous system.

In this patient, despite the unusual location of the tumor, its overall histological appearance closely resembled an intracranial meningioma. The tumor was characterized by lobulated growth of uniform spindle cells with abundant lightly eosinophilic cytoplasm, round or oval clear nuclei and indistinct cytoplasmic borders, often arranged in concentric onion-skin-like whorls even in the absence of psammoma bodies.

On immunohistochemical study, the spindled tumor cells showed diffuse and intense positivity for EMA and also moderate reactivity for cytokeratin and vimentin. The immunohistochemical profile of most intracranial meningiomas is characterized by consistent positive staining for vimentin and EMA (19–23). Reactivity for cytokeratin and S-100 protein is variable among intracranial meningiomas. According to Radley et al. (22) and Mackay et al. (3), about 28% of meningiomas stain positively for S-100 protein and 12–32% express cytokeratin (3,22), as was found in the present case. It has been reported that extracranial meningiomas usually show similar immunohistochemical profiles to the intracranial variants (13,14,24). Expression of E-cadherin is known to be characteristic of intracranial meningiomas (25,26), but this case was negative for E-cadherin.

Ultrastructurally, the tumor cells had bipolar cytoplasmic processes and were joined by small desmosomes, features almost consistent with those of intracranial meningioma. In the present case, however, the cell processes contained pinocytotic vesicles and were covered by a distinct external lamina, rather characteristic of the perineurial cells of a peripheral nerve (27). A discrete external lamina has also been described in a retroperitoneal meningioma (13), but not as a feature of intracranial meningioma (28).

Taking into account the anatomical location, the histological differential diagnosis should include benign and low-grade soft-tissue tumors with spindle cell morphology, such as Schwannoma, perineurioma and monophasic fibrous synovial sarcoma. Schwannoma is a tumor derived from Schwann cells. Its hallmark is a pattern arranged either compactly (Antoni A) or loosely (Antoni B), with short bundles, interlacing fascicles. An important characteristic of Schwannoma is the presence of consistently diffuse and strong expression of S-100 protein. Monophasic fibrous synovial sarcoma is a fibrosarcoma-like tumor and some tumor cells show positive staining for keratin and EMA, as was found in the present case. However, they consist of rather plump, spindle-shaped cells of uniform appearance with very small amounts of indistinct cytoplasm. Perineurioma is a rare soft-tissue tumor composed of pure perineurial cells devoid of residual axons and Schwann cells. The tumor cells, which show more elongated bipolar cytoplasmic processes, by light microscopy, than do meningothelial cells, tend to be arranged in intersecting fascicles or a storiform pattern and occasionally form tactile corpuscle-like and Verocay-like structures. Positive immunostaining for EMA and vimentin as well as lack of staining for S-100 protein and cytokeratin and ultrastructural perineurial cell features are characteristic of perineurioma (29,30).

There are several explanations for the histogenesis of extracranial meningiomas. In the head and neck region, these tumors are often associated with cranial nerves and appear to be derived from ectopic arachnoid tissue (2,31). It has been suggested that ectopic lung meningiomas arise from ectopic arachnoid cells (17,32) or from mesenchymal cells or Schwann cells that have differentiated into meningothelial cells (24). Recent studies have shown that arachnoid cells and perineurial cells, commonly expressing EMA, may be embryologically and functionally related (33). The perineurium of the peripheral nerve is continuous with the arachnoid membrane and the perineurial cells are thought to be functionally similar to arachnoid cells, despite some morphological and functional differences (34). It is, therefore, theoretically possible that

Figure 4. Immunohistochemistry of a primary extracranial meningioma of the foot. Most of the neoplastic cells show diffuse and intense reactivity for epithelial membrane antigen (a) and cytokeratin (b).
Figure 5. Ultrastructure of a primary extracranial meningioma of the foot. Tumor cells are predominantly spindle-shaped with thin bipolar cytoplasmic processes and oval nuclei and are covered by a distinct external lamina on both free surfaces (original magnification ×4000).

Figure 6. Ultrastructure of a primary extracranial meningioma of the foot. Pinocytotic vesicles and external lamina are observed frequently on the cell surfaces (arrows; original magnification ×17 000). The cytoplasmic processes are joined by multiple small desmosomes (arrowheads and inset; original magnification of inset ×36 000).

some ectopic meningiomas may be derived from perineurial cells rather than from displaced arachnoid cells. In this case, the immunohistochemical and ultrastructural studies were similar to the features of perineurioma. We have also tried to
immunostain for E-cadherin in four cases of perineurioma which we have in our files, but all cases of perineurioma were negative for E-cadherin (data not shown). The results of immunohistochemical and ultrastructural studies, intermediate between those of intracranial meningiomas and perineuriomas, suggest that soft-tissue meningiomas and perineuriomas may be closely related but morphologically distinguishable neoplasms.

With regard to the malignant potential of this case, because the tumor contained foci of necrosis and mitotic figures were 4/10 HPF, we think that careful long-term follow-up is required. The non-homogeneous gadolinium staining pattern of this tumor in MRI might show the presence of necrotic areas, but the corresponding necrotic areas were microscopically minimal. There are a few reports describing aggressive behavior of extracranial meningiomas (3,13) and a lethal case of low-grade malignant perineurioma transforming into a high-grade malignancy after long incipient period (35).

In summary, primary ectopic meningioma is a rare neoplasm. It can be identified by its characteristic morphology and immunoprofile and should be included in the differential diagnosis of soft-tissue spindle-cell tumors, especially those of peripheral nerve origin. In view of the mitotic figures and foci of necrosis identified in the present tumor, careful long-term follow-up is required.

References